Attorney's Docket No. 9310-13DVCTDV PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Middeldorp et al.
Serial No.: To be assigned
Filed: Concurrently herewith
For: PEPTIDES AND NUCLEIC ACID SEQUENCES RELATED TO THE EPSTEIN BARR VIRUS

Date: December 21, 2001

BOX PATENT APPLICATION
Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Sir:

Please enter the following Preliminary Amendment before examining the present application.

In the Specification.

On page 1, after the title, please insert the following text:

-- RELATED APPLICATION INFORMATION

This application is a divisional application of co-pending United States Application Serial No. 09/205,169, filed December 4, 1998 (now allowed); which is a continuation of prior United States Application Serial No. 08/415,838 filed April 3, 1995, now United States Patent No. 6,008,327; which is a divisional of prior United States Application Serial No. 08/031, 148, filed March 12, 1993, now United States Patent No. 5,424,398.; the disclosures of which are incorporated by reference herein in their entireties.

FIELD OF THE INVENTION --.

On page 1, between the first and second paragraph (before "EBV is an ubiquitous human herpes"), please insert the following centered text:

-- BACKGROUND OF THE INVENTION --

Please replace the sentence on page 5, line 14, with the following:

The viral capsid antigens (VCA) of EBV.

On page 7, between lines 4 and 5 (before "For the development"), please insert the following centered text:

-- BRIEF SUMMARY OF THE INVENTION --

On page 7, please amend the third paragraph as follows:

The present invention provides peptides comprising at least part of the VCA-p18 or VCA-p40 protein, encoded within the EBV open reading frames BFRF3 and BdRF1 respectively, and fragments thereof, immunochemically reactive with antibodies to the Epstein Barr Virus. Part of the invention are therefore peptides with 176 and 345 amino acids respectively and an amino acid sequence as shown in SEQ ID NO: 2 and 4 which are immunochemically reactive with EBV antibodies.

On page 7, before the last two lines on the page (before "The term 'peptide'"), please insert the following centered text:

-- DETAILED DESCRIPTION OF THE INVENTION --.

On page 15, please amend the second paragraph as follows

Antibodies, directed to a peptide according to the invention are also part of the present invention. The peptides or fragments thereof prepared and described above are used to produce antibodies, both polyclonal and monoclonal. Monoclonal antibodies directed against peptides according to the invention can be readily produced by one skilled in the art. Preferred antibodies to different epitopes of the VCA-p18 protein according to the invention are antibodies produced by the rat-mouse hybridoma cell line deposited at the European Culture of Animal Cell Cultures (ECACC) CAMR, Porton Down, Salisbury, Wilt. SP4 OJG, UK, under the deposit nos. 93020413 or 93020412, both deposited on February 4, 1993. Preferred antibodies having the same reactivity with VCA-p40 as antibodies produced by the mouse-mouse hybridoma cell line deposited at the European Culture of Animal Cell Cultures (ECACC) CAMR, Porton Down, Salisbury, Wilt. SP4 OJG, UK, under the provisional deposit no. 93020414, deposited on February 4, 1993.

On page 20, line 18, in the third paragraph (just before "Figure 1:"), please delete the line reading "LEGENDS:" and replace with the following, centered on the line:

--BRIEF DESCRIPTION OF THE FIGURES--

On page 22, in the second paragraph (beginning at "Peptide 1:"), please amend the text as follows:

Peptide 1: H_2N-GVPRRQRAIDKRQRA-COOH as shown in SEQ ID No. 7.

Peptide 2: H_2N-GQPHDTAPRGARKKQ-COOH as shown in SEQ ID No. 8.

Peptide 3: H_2N-AVDTGSGGGGQPHDTAPRGARKKQ-COOH as shown in SEQ ID No. 5.

Peptide 4: H_2N-STAVAQSATPSVSSSISSLRAATSGATAAA-COOH as shown in SEQ ID No. 6.

Peptide 5: Combi-peptide of peptide 4 and 3 linked by S-S-bridging.

On page 32, line 7, please replace the table with the following rewritten table:

--

Serum No.	Domain I (pept. 120-140)		
	Elisa OD_{450}	Peptide A.A. – sequence	
1	1.418	120-TAVAQSATPSVS-132	**SEQ ID NO:9**
2	1.820	120-TAVAQSATPSVS-132	**SEQ ID NO:9**
3	1.228	128-PSVSSSISSLRA-140	**SEQ ID NO:10**
4	1.230	128-PSVSSSISSLRA-140	**SEQ ID NO:10**
5	0.540	128-PSVSSSISSLRA-140	**SEQ ID NO:10**
6	0.731	129-SVSSSISSLRAA-141	**SEQ ID NO:11**
7	0.385	129-SVSSSISSLRAA-141	**SEQ ID NO:11**
8	1.360	131-SSSISSLRAATS-143	**SEQ ID NO:12**
9	1.598	131-SSSISSLRAATS-143	**SEQ ID NO:12**
10	1.591	131-SSSISSLRAATS-143	**SEQ ID NO:12**
11	1.251	131-SSSISSLRAATS-143	**SEQ ID NO:12**
12	1.839	133-SISSLRAATSGA-145	**SEQ ID NO:13**
13	1.128	134-ISSLRAATSGAT-146	**SEQ ID NO:14**
14	1.064	138-RAATSGATAAAS-150	**SEQ ID NO:15**
15	0.695	138-RAATSGATAAAS-150	**SEQ ID NO:15**

Serum No.	Domain II (pept. 152-155)		
	Elisa OD_{450}	Peptide A.A. – sequence	
1	-	-	-
2	0.678	155-DTGSGGGGQPHD-167	**SEQ ID NO:19**
3	-	-	-
4	-	-	-
5	-	-	-
6	-	-	-
7	-	-	-
8	-	-	-
9	0.510	153-AVDTGSGGGGQP-165	**SEQ ID NO:17**
10	0.474	153-AVDTGSGGGGQP-165	**SEQ ID NO:17**
11	0.958	152-AAVDTGSGGGGQ-164	**SEQ ID NO:16**
12	-	-	-
13	0.460	154-VDTGSGGGGQPH-166	**SEQ ID NO:18**
14	-	-	-
15	-	-	-

Serum No.	Domain III (pept. 159-165)		
	Elisa OD_{450}	Peptide A.A. – sequence	
1	-	-	-
2	0.423	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
3	0.808	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
4	0.761	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
5	1.354	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
6	1.441	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
7	0.770	163-QPHDTAPRGARK-175	**SEQ ID NO:22**
8	1.343	160-GGGQPHDTAPRG-172	**SEQ ID NO:20**
9	1.481	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
10	1.481	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
11	0.774	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
12	0.407	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
13	1.535	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
14	1.319	162-GQPHDTAPRGAR-174	**SEQ ID NO:21**
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On page 34, in the second paragraph (after "Peptides used were:"), please amend the text as follows:

Peptide 1: H_2N-GVPRRQRAIDKRQRA-COOH as shown in SEQ ID No. 7.

Peptide 2: H_2N-GQPHDTAPRGARKKQ-COOH as shown in SEQ ID No. 8.

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Peptide 4: H_2N-STAVAQSATPSVSSSISSLRAATSGATAAA-COOH as shown in SEQ ID No. 6.

Peptide 5: Combi-peptide of peptide 4 and 3 linked by S-S-bridging, using extra cysteine residues at the C-terminus of peptide 4 and the N-terminus of peptide 3.

On page 48, in line 1 (just before Claim 1), please delete the line reading "Claims:" and replace it with the following text:

--THAT WHICH IS CLAIMED IS:--

In the Abstract

After page 50, please insert page 51, "Abstract of the Disclosure," provided on a separate sheet and attached hereto in accordance with MPEP § 608.01(b).

In the Claims.

Please cancel Claims 1-5, 10-22, and 24. These claims were pursued in the parent applications or are drawn to non-elected inventions.

Please amend the claims as follows:

6. (Amended) Nucleic acid sequence encoding a peptide immunochemically reactive with antibodies to the Epstein Barr Virus (EBV), comprising at least part of the VCA-p18 or VCA-p40 protein, encoded within the EBV open reading frames BFRF3 and BdRF1, respectively, or a functional variant thereof.

9. (Amended) A recombinant vector molecule comprising a nucleic acid sequence according to claim 6.

23. (Amended) Method for the amplification and the detection of an Epstein-Barr Virus nucleic acid sequence in a sample using at least one nucleic acid sequence or fragment thereof according to claim 6 as primer(s) in order to perform a nucleic acid amplification of said Epstein-Barr Virus nucleic acid sequence and to detect the amplified sequence.

Please add the following new claims:

26. A recombinant vector molecule comprising a nucleic acid sequence according to Claim 7.

27. A recombinant vector molecule comprising a nucleic acid sequence according to Claim 8.

28. Method for the amplification and the detection of an Epstein-Barr Virus nucleic acid sequence in a sample using at least one nucleic acid sequence or fragment thereof according to claim 7 as primer(s) in order to perform a nucleic acid amplification of said Epstein-Barr Virus nucleic acid sequence and to detect the amplified sequence.

29. Method for the amplification and the detection of an Epstein-Barr Virus nucleic acid sequence in a sample using at least one nucleic acid sequence or fragment thereof according to claim 8 as primer(s) in order to perform a nucleic acid amplification of said Epstein-Barr Virus nucleic acid sequence and to detect the amplified sequence.

Remarks

Attached hereto is a marked-up version of the changes made to the claims and specification, entitled **"Version with Markings to Show Changes Made"**.

Conclusion.

Claims 6-9, 23 and 25-29 are pending following entry of the amendment herein. Applicants respectfully submit that this application is in condition for substantive examination, which action is respectfully requested.

Respectfully submitted,

Karen A. Magri
Registration No. 41,965

Enclosures: Version with Markings to Show Changes Made
Abstract of the Disclosure

Customer Number:

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PATENT TRADEMARK OFFICE

CERTIFICATE OF EXPRESS MAILING

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I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: BOX PATENT APPLICATION, Commissioner for Patents, Washington, DC 20231.

Traci A. Brown

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims.

6. (Amended) Nucleic acid sequence encoding a peptide [according to any of claims 1-5] immunochemically reactive with antibodies to the Epstein Barr Virus (EBV), comprising at least part of the VCA-p18 or VCA-p40 protein, encoded within the EBV open reading frames BFRF3 and BdRF1, respectively, or a functional variant thereof.

9. (Amended) A recombinant vector molecule comprising a nucleic acid sequence according to [any of claims 6-8] claim 6.

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[**LEGENDS:**] BRIEF DESCRIPTION OF THE FIGURES

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[Claims:] THAT WHICH IS CLAIMED IS:

In the Claims.

Please cancel Claims 1-5, 10-22, and 24. These claims were pursued in the parent applications or are drawn to non-elected inventions.

Please amend the claims as follows:

6. (Amended) Nucleic acid sequence encoding a peptide [according to any of claims 1-5] immunochemically reactive with antibodies to the Epstein Barr Virus (EBV), comprising at least part of the VCA-p18 or VCA-p40 protein, encoded within the EBV open reading frames BFRF3 and BdRF1, respectively, or a functional variant thereof.

9. (Amended) A recombinant vector molecule comprising a nucleic acid sequence according to [any of claims 6-8] claim 6.

23. (Amended) Method for the amplification and the detection of an Epstein-Barr Virus nucleic acid sequence in a sample using at least one nucleic acid sequence or fragment thereof according to [claim 6-8] claim 6 as primer(s) in order to perform a

nucleic acid amplification of said Epstein-Barr Virus nucleic acid sequence and to detect the amplified sequence.

Please add the following new claims:

26. A recombinant vector molecule comprising a nucleic acid sequence according to Claim 7.

27. A recombinant vector molecule comprising a nucleic acid sequence according to Claim 8.

28. Method for the amplification and the detection of an Epstein-Barr Virus nucleic acid sequence in a sample using at least one nucleic acid sequence or fragment thereof according to claim 7 as primer(s) in order to perform a nucleic acid amplification of said Epstein-Barr Virus nucleic acid sequence and to detect the amplified sequence.

29. Method for the amplification and the detection of an Epstein-Barr Virus nucleic acid sequence in a sample using at least one nucleic acid sequence or fragment thereof according to claim 8 as primer(s) in order to perform a nucleic acid amplification of said Epstein-Barr Virus nucleic acid sequence and to detect the amplified sequence.

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